Intracranial and Extracranial Aneurysms in a Patient with Neurofibromatosis Type 1: An Unusual Association: Case Report

Nörofibromatozis Tip 1'de İntrakraniyal ve Ekstrakraniyal Anevrizma: Alışılmadık Bir Birliktelik

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ABSTRACT Although the diagnosis of neurofibromatosis type 1 (NF-1) is an easy one, intensive monitoring of the patients is an obligation as various complications may develop leading to serious morbidity, even mortality by the time. NF-1 is usually associated with a variety of localized or systemic manifestations. Among them vascular dysplasia of intracranial arteries is an extremely rare one, which is even rarer as the presenting manifestation at the time of diagnosis. In the relevant literature multiple aneurysm formations in both intracranial and extracranial vascular structures are mentioned. Carotid artery and vertebral artery aneurysms, or hepatic artery and superior mesenteric artery aneurysms are examples of such associations. In this paper a patient who was diagnosed as definite NF-1 on the basis of more than six café-au-lait spots larger than 1,5 cm each, more than two neurofibromas, axillary freckling, and two first-degree relatives with the same diagnosis was reported in whom co-existence of aneurysms in the right middle cerebral artery and the right renal artery was found.

Key Words: Neurofibromatosis 1; intracranial aneurysm; renal artery

ÖZET Nörofibromatozis tip 1 (NF1), tanısı güçlük oluşturmayan, ancak yıllar içinde ortaya çıkan çeşitli komplikasyonlar nedeniyle hastaların özenle takibini gerektiren bir klinik tablodur. NF1'de lokalize ve sistemik belirtilerin çeşitliliği mevcuttur. Bunlar arasında nadir görülen bir durum olan serebrovasküler displazi NF1'in ilk belirtisi olabilir. Literatürde intrakraniyal ve ekstrakraniyal arteryel yapılarda birden fazla sayıda anevrizma oluşumundan söz edilmiştir. Karotis ve vertebral arter anevrizmaları ile hepatik ve superior mezenterik arter anevrizmaları bu birliktteliklere örnek teşkil eder. Bu olgu raporunda, 1,5 cm'den geniş ve altıdan fazla café-au-lait lekesi, ikiden fazla nörofibrom, aksiller çillenme ve birinci derece iki akrabada aynı tanı olması nedeniyle NF1 tanısı alan olguda saptanan orta serebral arter ve renal arter anevrizmalarının birlikteliği sunulmuştur.

Anahtar Kelimeler: Nörofibromatozis 1; intrakranial anevrizma; renal arter

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Neurofibromatosis type 1 is a hereditary disease with an autosomal dominant pattern. It is classified within the phakomatoses group.[1] NF-1 gene which is located in the 17th chromosome (17q.11.2) encodes neurofibromin protein which has tumor suppressing function.[2] Mutations in this gene are held responsible for tumors emerging in various tissues. The disease is characterized with skin features like cutaneous pigmentations, freckling in the axilla, neurofibromas and other tumors.[3] In addition both cerebral and peripheral vascular structures may be involved in different forms. As well as arterial stenoses and occlusions, aneurysm for-

mations, arteriovenous malformations, and arteriovenous fistulas may be seen.[4,5] In this paper a patient with newly diagnosed NF-1 who presented with aneurysms in the middle cerebral and renal arteries will be discussed.

CASE REPORT

Sixty-five years old male patient was brought to the emergency department because of a generalized tonic clonic convulsion. During the emergency follow-up he experienced a secondary generalized epileptic seizure beginning from left side of the face and the body. In the past history of the patient hypertension and left sided weakness for six years were noted.

In the neurologic examination, in addition to dysarthria and left hemiparesis multiple neurofibromas, café-au-lait spots, bilateral axillary freckles and scoliosis were observed (Figure 1). Total blood count, routine biochemistry, chest X-ray and an electrocardiogram (ECG) were normal. An electroencephalogram (EEG) revealed remarkable slowing of the basic rhythms at the anterior part of the right hemisphere with a preponderence of theta and slight delta activity. Chronic ischemic changes were detected in the right posterior parietal region at the computerized tomography (CT) and magnetic resonance imaging (MRI) of the brain. Neuroimaging also revealed a calcified and thrombosed aneurysm of possibly the right middle cerebral artery. CT angiography (CTA) and MR angiography (MRA) of the brain confirmed the origin of the aneurysm as the right middle cerebral artery (Figures 2, 3). In order to search for additional occult tumors or aneurysms, cervical and thoracic spinal cord and abdominal organs were examined radiologically. An aneurysm of the right renal artery reaching 2 cm in diameter was found at the CTA of the abdomen (Figure 4). The patient did not give his informed consent for a digital subtraction angiography (DSA) and was discharged under antiepileptic and antihypertensive medications. No intervention for the aneurysms was planned except regular follow-ups.

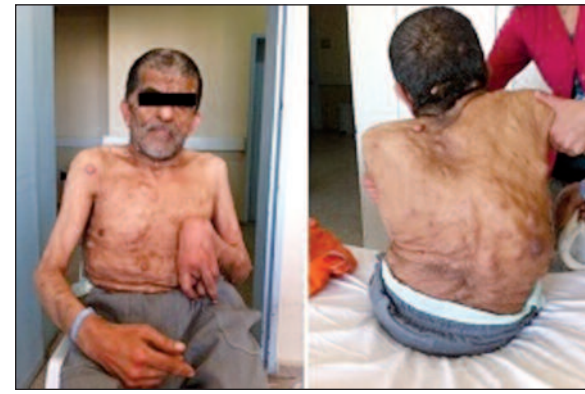

FIGURE 1: Multiple neurofibromas, multipl café-au-lait spots, bilateral axillar freckles and scoliosis were observed.

DISCUSSION

Neurofibromatosis type 1 is a disease which is not hard to diagnose. Central and peripheral nervous system tumors, hamartomas, dysplastic myelination areas of the white matter and deformities of the skeletal system are well-known features.[6] Serious complications like vascular dysplasias may be

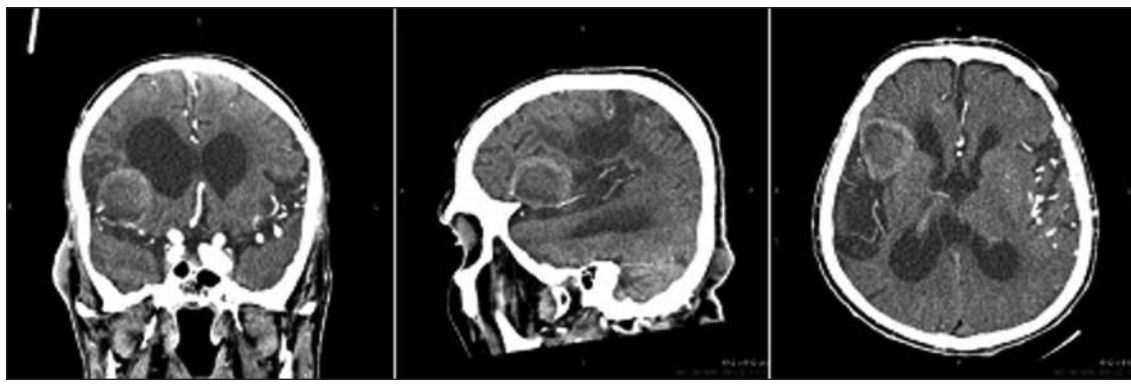

FIGURE 2: Approximately 3 cm diameter, calcified, thrombosed middle cerebral artery aneurysm and chronic ischemic changes were detected in right posterior parietal region with computerized tomography angiography.

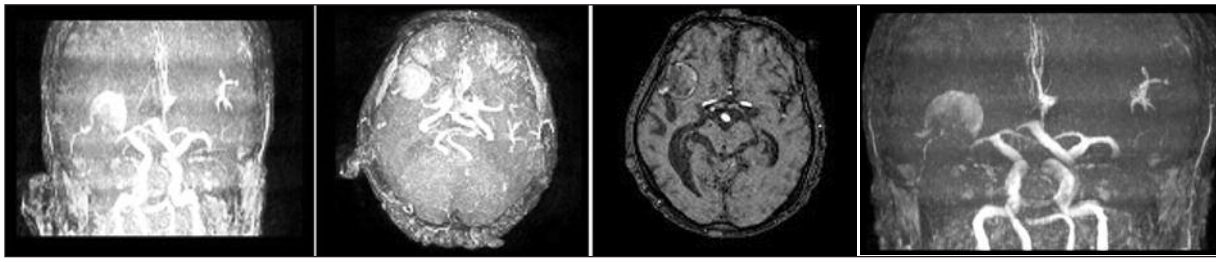

FIGURE 3: Aneursym confirmed the origin of the aneurysm as the right middle cerebral artery by using 3D time-of-flight (TOF) and maximum intensity projection (MPI) in magnetic resonance angiography.

encountered in 2-5% of the NF-1 cases. Hypertension, stroke or subarachnoidal bleeding may also develop during the disease course.[7] Intimal proliferation, vessel wall thickening, stenosis or medial layer defects are well-defined vascular histopathologic findings as well as aneurysm formations in both central and peripheral nervous arterial systems. Vascular involvement in NF-1 is connected to neurofibromin deficiency.[4,5]

Our patient had a left hemiparesis of six years old which was probably due to a left parietal infarct. Apparently hypertension is a predictable risk factor for the development of this infarct. However in differential diagnosis additional possibilities exclusive to our patient, must be mentioned like vascular bed involvement with NF-1.[8] A mass effect of the aneurysm by pressing the relevant artery, thus leading ischemia is another explanation. An embolus originating from the thrombus in the aneurysm is a speculation with comparatively low probability. Internal carotid artery is the most frequently involved artery by cerebrovascular dysplasia, middle cerebral artery the second.[9] Hence an infarct due to vascular involvement of the middle cerebral artery by NF-1 seems the most plausible explanation in our patient.

The patient was brought to emergency service because of generalized tonic clonic convulsions. No overt epileptogenic focus was detected in the EEG. However in the right anterior hemisphere remarkable focal slowing of the basic rhytms was observed which was regarded as a proof of an epileptogenic area in the right hemisphere.

Arterial hypertension develops in 6% of NF-1 patients.[10] In that case aortal coarctation, pheochromocytoma, renal arterial stenosis or an aneurysm of the renal artery may be the cause of hypertension.[11,12] Multiple aneurysms or aneurysm-stenosis associations are reported in NF-1 patients.[13] In our patient CTA examination of renal arteries revealed an aneurysm of the left renal artery which may be etiologically linked to hypertension. Although a DSA was offered in order to examine the vascular bed of the kidneys and the aneurysm better, and to search for a stenotic lesion, the patient did not approve the procedure.

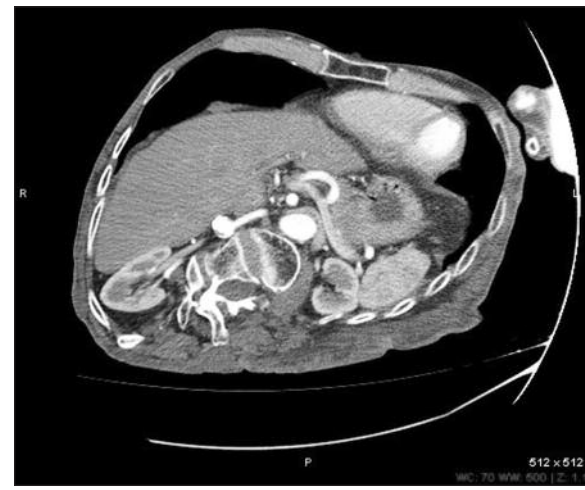

FIGURE 4: Approximately 2cm diameter, right renal artery saccular aneurysm was found at CTA of the abdomen.

In different sources the associations of multiple aneurysms in intra- and extracranial vessels are mentioned.[5] Carotid artery and vertebral artery aneurysms, or hepatic artery and superior mesenteric artery aneurysms are such associations. However we couldn't find any publication reporting co-existence of aneurysm formations in intracranial and distant extracranial arteries. Hence our patient is worthy of presentation.

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